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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/773,599

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John Craig Smith

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FISH & RICHARDSON PC  
225 FRANKLIN ST  
BOSTON, MA 02110

EXAMINER

SWITZER, JULIET CAROLINE

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/773,599	SMITH, JOHN CRAIG	
	<b>Examiner</b>	<b>Art Unit</b>	
	Juliet C. Switzer	1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 January 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 6-15 and 17-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 16 and 23 is/are rejected.
- 7) ☒ Claim(s) 4 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of Group II, claims 1-5 and 16 with traverse is acknowledged (see paper filed 1/15/2003). Applicant's further election of the single polymorphism at position 33251 of the reverse complement of EMBL Accession AC006953, with traverse is also acknowledged. Further, Applicant's addition of claim 23 is acknowledged. Claim 23, which encompasses the method of claim 1, will be examined with the elected group.
2. Applicants object to the amended restriction requirement, especially with respect to restricting eight polymorphisms into eight separate groups, stating that in view of the addition of claim 23 the restriction requirement is improper. However, this is not persuasive. The restriction requirement which indicates that methods which require the diagnosis of only one of the eight recited polymorphisms remain separate and distinct from one another, even if they are each not separate and distinct from a method which examines all of them. Applicant has provided no reasoning to support their position, and thus the previously set forth requirement concerning claims which only require one of the eight polymorphisms recited in the claims is maintained and made FINAL.

### ***Specification***

3. The title is objected to because it does not clearly reflect the subject matter of the elected invention. A title such as "Detection of polymorphisms in the human uPAR gene" would be more appropriate.
4. The disclosure is objected to because of the following informalities: The specification and claims repeatedly refer to EMBL accession numbers instead of reciting sequences or

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sequence identifiers. This recitation is similar to the recitation of a trademark, in that the EMBL accession number does not represent a fixed disclosure of a sequence, but instead refers to a record that is constantly able to be updated and modified. Applicant should amend the specification to include the sequences which are referred to by EMBL accession numbers (and comply with the remainder of the sequence rules) and file a 132 declaration with evidence showing and stating that the newly filed sequence is identical to the sequence that was in EMBL at the time the invention was filed.

#### ***Claim Objections***

5. Claim 4 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from a previous multiple dependent claim. In this case, claim 4 depends from claim 3 which is also a multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

#### ***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2, 3, 4, 5, 16, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 16 are is indefinite over the recitation “determining the sequence of the nucleic acid of the human at one or more of positions...” because it is unclear how you determine a sequence at a single position of a nucleic acid. The word “sequence” implies the

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determination of the nucleotide present at more than one position of a nucleic acid, yet the claims set forth that the sequence is determined at one or more of the recited positions. It is not clear how a sequence can be determined at a particular position. Amendment of the claim to recite, for example, "determination of the nucleotide present at position 33251 of the reverse complement of EMBL Accession Number AC006953" would obviate this rejection. Claims 2, 3, 4, 5, and 23 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

Claims 1 and 16 are indefinite over the recitation "of the reverse complement of EMBL Accession number...." because it is not clear what is intended by the "reverse complement." Biologically speaking, the nucleic acid disclosed in the EMBL record is presented 5' to 3'. That is, give the sequence ATG in the disclosure, the A is at the 5' end of the nucleic acid while the G is at the 3' end. The biological complement of this molecule is therefore 5' to 3', CAG. It is unclear what the "reverse complement" is, as this is not a phraseology which has any biological meaning.

Claims 1 and 16 are indefinite over the recitation of EMBL accession numbers (AC006953) because it is not clear as to what is encompassed by this phrase. The sequences listed in the EMBL database are continuously updated and modified. Therefore, there is no single, fixed definition for the sequences presented as EMBL Accession AC006953. Claims 2, 3, 4, 5, and 23 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

Claims 1 and 16 are further indefinite over the recitation "determining the status of the human by reference to polymorphism" because it is not clear what this step is requiring. It is not

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clear what it means to determine the status of a human "by reference to polymorphism." Claims 2, 3, 4, 5, and 23 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

In claim 3, the phrase "the potential single nucleotide polymorphism" lacks proper antecedent basis in the claims because the claims do not previously refer to a "potential" polymorphism.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5, 16, and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting and sequencing the urokinase plasminogen activator receptor (uPAR) gene and portions thereof, does not reasonably provide enablement for methods which are limited to the detection of a polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953. Furthermore, the specification does not provide enablement for methods in which a polymorphism is diagnosed and then a uPAR ligand antagonist drug is administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This rejection applies to the instant claims insofar as they might be interpreted as methods for the detection of the presence or absence of particular single nucleotide polymorphisms. It applies to claim 12 insofar as the claim implies that there would be a

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connection between the step of detection of the polymorphism and the administration of the uPar ligand antagonist drug. Insofar as the instant claims read generally on methods for sequencing the human urokinase plasminogen activator receptor (uPAR ) gene, this rejection does not apply. The teachings of the specification (at, e.g., page 20-21) and of the prior art as exemplified by Wang et al. disclose methods of detecting and sequencing the uPAR gene and portions thereof. Such methods are encompassed by the instant claims as written, and a person skilled in the art could clearly practice methods of detecting and sequencing a known gene without further guidance. However, it is unpredictable as to whether one of skill in the art could use without undue experimentation methods requiring detection of the polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953 or methods for treatment which comprise detection of the polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953, which methods are also encompassed by the claims. Furthermore, it is unpredictable as to whether one of skill in the art could use without undue experimentation a method which requires the examination of eight different single nucleotide polymorphisms in the uPAR gene.

It is noted that the instant claims each recite methods which comprise the detection of nucleotide sequences at one or more of ten different polymorphic sites. A restriction requirement was set forth in which applicant was required to select a single polymorphic site for examination. Applicant selected the polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953. This enablement rejection considers only this site in the claims that recite polymorphisms in the alternative. With regard to claim 23, many of the examples in this rejection are directed at the elected polymorphism, but it is to be understood that

the rejection applies to claim 23 also which requires the examination of eight different polymorphic sites.

The instant claims are drawn to methods for the diagnosis of a polymorphism in an uPAR gene in a human. The methods comprise steps in which the particular nucleotide is detected at a particular position in different portions of the human uPAR gene. Claim 16 further comprises a step in which a uPAR ligand antagonist drug is administered in an "effective amount."

The specification teaches that uPAR "plays a key role in cancer cell invasion and metastasis, controlling cell motility, tissue remodeling and the bioavailability of angiogenic factors (p. 1)." The specification further teaches that uPAR antagonists may have some clinical utility in diseases such as diabetic retinopathy, corneal angiogenesis, Kaposi's syndrome, metastasis and invasion by tumor cells, chronic inflammation and the like (p. 8). Thus, the genus of disease considered within the "uPAR mediated diseases" is quite large. Further, the specification provides ten polymorphisms in the uPAR gene. In particular, the specification teaches a polymorphic site at position 33251 of the reverse complement of EMBL Accession Number AC006953, located within exon 6 of the uPAR gene. The specification teaches that the polymorphism results in an amino acid change from LYS to ARG at position 198 of the encoded polypeptide, and also results in the formation of a PstI restriction site in uPAR nucleic acid, and that this nucleic acid is within a "functional domain" of the protein (p. 5). The specification is silent with respect to the effect of this polymorphism on the biological activity of the uPAR gene, or the effect of any of the other 9 recited polymorphisms on the biological activity of the gene. The specification does not disclose any relationship between the presence of this



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polymorphism a change in the activity or expression of the uPAR or between the presence of a particular allele of this polymorphism and any particular disease state or physiological condition.

The prior art provides two polymorphisms in the coding portion of the uPAR gene. Børglum et al. (Human Genetics (1992) 89:584) teach two polymorphisms within the coding region of the uPAR gene (referred to therein as PLAUR). These both result in the formation of loss of a PstI restriction site. Børglum *et al.* are silent as to the effects of these polymorphisms on the encoded polypeptide. The prior art does not provide specific guidance with regard to the polymorphism identified herein as being at position 33251 of the reverse complement of EMBL Accession Number AC006953, or any of the other polymorphism identified herein, whose examination is required by claim 23.

There is also a large body of knowledge in the prior art related to polymorphisms in general, and their association with diseases or disease states. The art is highly unpredictable with regard to the functionality of polymorphic sites in genomic DNA. After a screening assay identifies polymorphisms, it is unpredictable whether any such polymorphisms would be associated with any phenotypic trait, such as a disease state or a physiological state. For example, Hacker et al. were unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (Gut, 1997, Vol. 40, pages 623-627). Even in cases where an association between a particular gene and a disease state is known to exist, such as with the LPL gene and heart disease risk or the  $\beta$ -globin gene and sickle cell anemia, researchers have found that when using SNP (single nucleotide polymorphism analysis) it was difficult to associate SNPs with disease states or to even identify key genes as being

associated with disease (Pennisi, Science, 281 (5384):1787-1789). Finally, in some cases where multiple polymorphisms are identified in a gene, some of these are demonstrated to be disease associated and some are not. Blumenfeld et al. (WO 99/52942) disclose a number of polymorphisms in the FLAP gene. While Blumenfeld et al. were able to demonstrate that some of these polymorphisms are associated with patients having asthma but some of these are not (see Figure 3). For example, the marker 10-35/390 was demonstrated to be associated with asthma, with a p value of 0.00229, while the marker 10-33/327 was determined to not have a statistical association with asthma ( $p=0.294$ ). Thus, even for SNPs within the same gene, it is highly unpredictable as to whether a particular marker will be disease associated.

The level of skill in the pertinent art is quite high, i.e. generally a PhD in biochemistry, but the unpredictability in the art is higher. While the instant specification has disclosed a number of different polymorphisms in the uPAR gene, it remains highly unpredictable as to the biological significance of these polymorphisms. The specification postulates that SNPs within the protein coding sequence "may give rise to the expression of a variant protein and, potentially, a genetic disease (p. 2)," but the specification does not set forth which genetic disease. Thus, the claimed method directed towards the diagnosis of polymorphisms, or treatment of disease following diagnosis of polymorphisms, for enablement of the full scope, requires the knowledge of unpredictable and potentially non-existent associations between the instantly elected polymorphism and some phenotypic trait. Even if the elected polymorphism is in some way associated with some disease, it is difficult (if not impossible) to know or predict from the teachings of the specification which disease or how the polymorphism is associated. That is, it is unpredictable as to whether the presence of a particular allele the polymorphism

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would confer a higher or lower likelihood of having the disease. In this case, the possible uses for the claimed methods are undefined, beyond the suggestion that they can be used to detect a disease associated with the uPAR gene prior to treatment with a uPAR ligand antagonist drug.

The amount of direction or guidance presented in the specification with regard to how to use the instant invention is minimal. Since the effects of any given polymorphism on gene activity are highly unpredictable, it is impossible to predict from the teachings of the instant specification what identifications can be made using the instantly claimed methods. That is, the specification does not provide any guidance as to how the polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953 would be associated with any pharmaceutical agent. The specification does not discuss whether this particular polymorphism will increase the likelihood of a positive or negative response to any drug. Furthermore, with regard to claim 16, which recites a method of treatment of a human in need of treatment with a uPAR ligand antagonist drug, the specification does not provide any guidance as to what disease is in fact associated with the presence or absence of the polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953, other than the suggestion that these methods could be carried out for "uPAR mediated diseases." The specification further fails to provide any guidance as to the appropriated uPAR drug to be administered after the detection of the polymorphism, or the desired effect of administration of the drug (i.e. to up or down regulate the activity of the gene, and how either of these is to be accomplished). The specification provides no guidance or working examples that teach or demonstrate the ability to use the disclosed polymorphic site as a marker for any disease in particular, or for disease in

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general, or how to use the disclosed polymorphism to select a proper course of treatment of a disease.

The quantity of experimentation required to discover how to use the instant invention is very high. In order to use the claimed invention, one would have to establish a relationship between the polymorphism at nucleotide 33251 of the reverse complement of EMBL Accession Number AC006953 some physiological or disease state or some disease treatment method. Indeed, even to use the method of claim 1 to identify patients suited for particular pharmaceutical agents, one would need to know that the polymorphism at nucleotide 33251 of the reverse complement of EMBL Accession Number AC006953 was in some way associated with response to some pharmaceutical agent. In order to obtain the type of information necessary to practice the claimed invention, one would be required to undertake the screening of hundreds or thousands of patients as well as possible hundreds of diseases or pharmaceutical agents. Even if such experiments were undertaken, it would still be unpredictable as to whether any associations would be detected, in light of the unpredictability of such associations, as already discussed. Thus, while one could perform further research to determine whether applicant's method would be useful in disease detection and/or treatment, it is unknown as to what the outcome of such research might be and as to whether any quantity of experimentation would result in the identification of an association between the A/G polymorphism at position 33251 and any disease or condition. Further, absent a teaching the A/G polymorphism at position 33251 is not associated with such conditions, it is further unpredictable as to whether detection of the A/G polymorphism at position 33251 would be useful in predicting, e.g., the absence or decreased likelihood of such conditions.

Furthermore, it is noted that the practice of the invention of claim 16 requires the administration of a uPAR ligand antagonist drug. The specification describes provides examples of such drugs (p. 8) but does not further describe or identify such drug. Thus, any drug, discovered or undiscovered that is an antagonist of uPAR is within the scope of the recitation of the claims. The specification does not disclose a relationship between treatment with these drugs and the polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953. The identification of a relationship between and the elected polymorphism would be highly unpredictable, requiring an extensive amount of research and experimentation.

Thus, in light of the nature of the invention, the state of the art, the high level of unpredictability in the art, the lack of direction or working examples in the specification, and the high quantity of experimentation that would be required to practice the claimed invention, it is concluded that undue experimentation would be required to use the instantly claimed invention. Thus, with respect to claims 1-5, and 23, although the specification certainly enables one to detect the presence of the polymorphism(s) (i.e. the "make" portion of 112 1<sup>st</sup> paragraph), it would require undue experimentation in order to determine how to use the methods of claims 1-5 and 23. It would also require undue experimentation to make and use the method of claim 16. Considering all of the factors discussed herein, it is concluded that it would require undue experimentation to determine the particular disease state that can be diagnosed and treated and thus to practice the claimed invention commensurate in scope with the present claims.

***Claim Rejections - 35 USC § 101***

10. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 4, 5, and 16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

It is noted that the instant claims each recite methods which comprise the detection of nucleotide sequences at one or more of thirteen different polymorphic sites. A restriction requirement was set forth in which applicant was required to select a single polymorphic site for examination. Applicant selected the polymorphism at position 33251 of the reverse complement of EMBL Accession Number AC006953. This utility rejection considers only this site in claims 4, 5, and 16.

The instant claims are drawn to methods for the diagnosis of a polymorphism in an uPAR gene in a human and methods for treatment of disease in which the polymorphism is identified and then a drug is provided. Each of the methods comprise steps in which the particular nucleotide present is detected at a particular position in the reverse complement of EMBL accession AC006953.

The specification teaches that the uPAR gene has been associated with a number of diseases and physiological states. Further, the specification provides ten polymorphisms in the uPAR gene. In particular, the specification teaches a polymorphic site at position 33251 of the reverse complement of EMBL Accession Number AC006953. The specification teaches that the disclosed polymorphism in exon 6 of the uPAR gene results in a change in the encoded amino acid sequence with a functional domain (p. 5). Furthermore, the specification suggests that the methods can be used to detect a uPAR mediated disease.

None of these asserted utilities meet the standard of being specific, substantial, and credible. Generally, these are utilities that can be assigned to a broad class of invention, that is any method for detecting a polymorphism, thus they are not specific. Furthermore, the utilities set forth are not considered to be substantial because further experimentation would be required to reasonably confirm that the disclosed polymorphism is in fact diagnostic or prognostic of disease or in fact associated with the suitability of a particular pharmaceutical agent. The specification merely postulates that such utilities exist, but in order to practice the claimed invention, further experimentation would be required to determine an association between the polymorphism and some physiological state or disease.

Claims 4, 5 and 16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The utility rejection has not been applied to claims 1-3 and 23 because these claims encompass an embodiment that would have utility, namely the sequencing of the uPAR gene, which itself is known to be associated with physiological and disease states. If the claims are narrowed to exclude this embodiment, these claims may be included in the utility rejection.

#### ***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 2 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (European Journal of Biochemistry, 1995, Vol. 227, pages 116-122).

Wang et al. teach a method for the diagnosis of a polymorphism in an uPAR gene in a human which comprises determining the sequence of the nucleic acid of the human at position 33251 of the reverse complement of EMBL Accession Number AC006953, and determining the status of the human by reference to polymorphism in the uPAR gene (p. 117 and Figure 2). Specifically, Wang et al. teach a method for sequencing the genomic uPAR gene (p. 310). This sequence inherently encompasses position 33251 of the reverse complement of EMBL Accession Number AC006953, as well as all of the additional positions recited in claim 23. This reference is considered to teach the invention of claims 1, 2, and 23 because the method contains only two method steps, one in which the sequence at position 33251 of the reverse complement of EMBL Accession Number AC006953 is determined (i.e. which is inherently accomplished by sequencing the portion of the gene that overlaps with position 33251 of the reverse complement of EMBL Accession Number AC006953 ), and one in which the "status of the human by reference to polymorphism" is determined. Determining the sequence of the gene is considered to inherently determine the status of the human by reference to the polymorphism because by sequencing the nucleotide present at position 1304, the status of the polymorphism is determined.

14. Claims 1, 2, and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Casey et al. (Blood, 1994, Vol. 84, pages 11561-1156).

Casey et al. teach a method for the diagnosis of a polymorphism in an uPAR gene in a human which comprises determining the sequence of the nucleic acid of the human at position



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33251 of the reverse complement of EMBL Accession Number AC006953, and determining the status of the human by reference to polymorphism in the uPAR gene (p. 1152). Specifically, Casey et al. teach a method for sequencing the genomic uPAR gene (p. 310). Casey *et al.* amplify the sequence using PCR prior to sequencing. This sequence inherently encompasses position 33251 of the reverse complement of EMBL Accession Number AC006953, as it is the coding sequence for uPAR. This reference is considered to teach the invention of claims 1, 2, and 3 because the method contains only two method steps, one in which the sequence at position 33251 of the reverse complement of EMBL Accession Number AC006953 is determined (i.e. which is inherently accomplished by sequencing the portion of the gene that overlaps with position 33251 of the reverse complement of EMBL Accession Number AC006953 ), and one in which the “status of the human by reference to polymorphism” is determined. Determining the sequence of the gene is considered to inherently determine the status of the human by reference to the polymorphism because by sequencing the nucleotide present at position 1304, the status of the polymorphism is determined.

15. Claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Børglum *et al.*

Børglum et al. teach a method for the diagnosis of a polymorphism in an uPAR gene in a human which comprises determining the sequence of the nucleic acid of the human at position 33251 of the reverse complement of AC006953, and determining the status of the human by reference to polymorphism in the uPAR gene. Specifically, Børglum et al. teach a method for the diagnosis of a polymorphism in a uPAR gene wherein the restriction enzyme PstI is used to identify a polymorphism in the coding sequence of the gene. The instant specification teaches

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that the polymorphism at position 33251 of the reverse complement of AC006953 is detectable by PstI. Thus, Børglum et al. inherently teach a method which determines the sequence at position 33251 of the reverse complement of AC006953 via RFLP analysis.

Applicant is reminded that MPEP 2112.01 teaches "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'" In the instant case, the method of the prior art is substantially identical to the instantly claimed method. The fact that the instant polymorphism results in a PstI site and the polymorphism disclosed by Børglum et al. is a PstI polymorphism is believed to be a sound basis for believing that the polymorphism disclosed herein is identical to one of the polymorphisms disclosed by Børglum et al. As such, the method for detecting the polymorphism taught by Børglum et al. inherently meets the limitations of the instantly rejected claims.

### ***Conclusion***

16. No claims are allowed.
17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is 703 306 5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

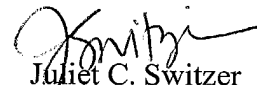
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703 308 1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305 3592 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0196.

  
Juliet C. Switzer  
Patent Examiner  
AU 1634

April 28, 2003

  
GARY BENZION, PH.D  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600